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Growth hormone receptor signalling.

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Abstract

The growth hormone (GH) receptor belongs to the superfamily of transmembrane proteins that includes the prolactin (PRL) receptor and a number of cytokine receptors. Two forms exist for the GH receptor: the membrane-bound form is a protein of 620 amino acid residues with a unique transmembrane domain; the GH-binding protein (GHP), which is a soluble short form, is identical to the extracellular domain of the membrane receptor. In man and many other species, GHP is believed to result from proteolytic cleavage of the membrane receptor; in human tissues, only one mRNA form of 4.5 kb encoding the full-length receptor has been detected. In rodents, GHP is encoded by a specific mRNA of 1.2kb. Binding of GH to its receptor results in dimerization of the receptor, phosphorylation of the tyrosine kinase JAK2 and of the receptor, followed by a cascade of protein phosphorylations. Transcription factors belonging to the signal transducers and activators of transcription (STAT) family are involved in the effects of GH on the transcription of genes such as c-fos, serine protease inhibitor Spi 2.1 and beta-casein. GH is able to activate several STAT proteins including STAT1, 3 and 5. The JAK-STAT pathway is a main pathway for GH effects on gene transcription. Other signalling molecules are involved in GH action through different pathways: GH is able to activate mitogen activated protein (MAP) kinases; the hormone can utilize insulin receptor substrate-1 (IRS-1) and induces the association of phosphatidylinositol 3-kinase with IRS-1. Two main functional regions have been defined in the cytoplasmic domain of the GH receptor by testing the activity of mutant forms of the receptor in several systems: Box 1, a proline-rich sequence in the membrane proximal part, is necessary for all GH effects and is probably the region of association with JAK2; the C-terminal region is required for the induction of specific genes. Other molecules involved in the mechanisms of action of GH remain to be identified. As the same signalling pathways are used by many ligands, explanations for the specificity of the cellular effects have to be determined.

MeSH

[Amino Acid Sequence](#); [Animal](#); [Ca\(2+\)-Calmodulin Dependent Protein](#)